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     (FILE 'HOME' ENTERED AT 10:44:42 ON 03 JUN 2008)
     FILE 'CA' ENTERED AT 10:45:23 ON 03 JUN 2008
L1   38170 S (DEPROTEI? OR DE PROTEI? OR PROTEIN?(3A)(REMOV? OR PRECIPITAT?))
L2    2665 S L1 AND(DRUG OR MEDICIN? OR PHARMACEUTI?)
L3     363 S L2 AND (MASS SPECTRO? OR MS MS)
L4      46 S L3 AND AUTOMAT?
L5      21 S L3 AND(AIDS OR HIV OR ANTIRETROVIRAL OR ANTIVIRAL OR RETROVIRAL
           OR VIRAL)
L6      23 S L3 AND(GENERAL OR GENERIC)
L7      28 S L3 AND(DRY? OR DRIED OR EVAPORAT? OR RECONSTITUT?)
L8     300 S L1(5A)COMPAR?
L9       6 S L3 AND L8
L10    104 S L4-7,L9
L11     40 S L10 AND PY<2003
L12      7 S L10 NOT L11 AND PATENT/DT
     FILE 'BIOSIS' ENTERED AT 10:53:18 ON 03 JUN 2008
L13     55 S L11
     FILE 'MEDLINE' ENTERED AT 10:53:58 ON 03 JUN 2008
L14     37 S L11
     FILE 'CA, BIOSIS, MEDLINE' ENTERED AT 10:54:52 ON 03 JUN 2008
L15     90 DUP REM L11 L12 L13 L14 (49 DUPLICATES REMOVED)

=> d bib,ab l15 1-90

L15  ANSWER 30 OF 90  CA  COPYRIGHT 2008 ACS on STN
AN   135:86474  CA
TI   Cassette-accelerated rapid rat screen: a systematic procedure for the
     dosing and liquid chromatography/atmospheric pressure ionization tandem
     mass spectrometric analysis of new chemical entities as part of new drug
     discovery
AU   Korfmacher, Walter A.; Cox, Kathleen A.; Ng, Kwokei J.; Veals, John;
     Hsieh, Yunsheng; Wainhaus, Sam; Broske, Lisa; Prelusky, Dan; Nomeir,
     Amin; White, Ronald E.
CS   Department of Drug Metabolism and Pharmacokinetics, Schering-Plough
     Research Institute, Kenilworth, NJ, 07033, USA
SO   Rapid Communications in Mass Spectrometry (2001), 15(5), 335-340
AB   This report addresses the continuing need for increased throughput in
     the evaluation of new chem. entities (NCEs) in terms of their
     pharmacokinetic (PK) parameters by describing an alternative procedure
     for increasing the throughput of the in vivo screening of NCEs in the
     oral rat PK model.  The new approach is called 'cassette-accelerated
     rapid rat screen' (CARRS).  In this assay, NCEs are dosed individually
     (n = 2 rats/compd.) in batches of six compds. per set.  The assay makes
     use of a semi-automated protein pptn. procedure for sample prepn. in a
     96-well plate format.  The liq. chromatog./atm. pressure ionization
     tandem mass spectrometry (LC/API-MS/MS) assay is also streamlined by
     analyzing the samples as 'cassettes of six'.  Using this new approach, a
     threefold increase in throughput was achieved over the previously
     reported 'rapid rat screen'.

L15  ANSWER 34 OF 90  CA  COPYRIGHT 2008 ACS on STN
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AN 135:352294 CA
TI Simple and rapid liquid chromatographic-turbo ion spray mass spectrometric determination of topiramate in human plasma
AU Contin, M.; Riva, R.; Albani, F.; Baruzzi, A.
CS Laboratory of Clinical Neuropharmacology, University of Bologna, Institute of Neurology, Bologna, 40123, Italy
SO Journal of Chromatography, B: Biomedical Sciences and Applications (2001), 761(1), 133-137
AB The authors present a simple and fast method for the detn. of the novel antiepileptic drug topiramate in human plasma by HPLC coupled with turbo ion spray mass spectrometry. Plasma sample pre-treatment was based on simple deproteinization by MeCN. Liq. chromatog. anal. was carried out on a reversed-phase column (C18, 125×4 mm I.D., 5 μm) using MeCN-ammonium acetate buffer, pH 6.3 as the mobile phase, at a flow-rate of 0.8 mL/min. Retention time for topiramate was 2.1 min. The detector was a single quadrupole mass spectrometer coupled to a turbo ion spray ion source and a heated nebulizer probe, operating in the pos. ion mode. Ion source temp. was off; voltage was +5800 V; nebulizer and curtain gas flow-rates were 6 and 10 mL/min, resp. Calibration curves for topiramate were linear over the range 1 to 20 μg/mL. Abs. recovery ranged between 92 and 95%. Intra- and inter-assay precision was <4%. The present procedure, omitting extn. and drying steps, is faster and simpler than the previously reported anal. methods for topiramate and possesses adequate sensitivity for routine therapeutic drug monitoring in plasma from patients with epilepsy.

L15 ANSWER 40 OF 90 BIOSIS on STN
AN 2002:27049 BIOSIS
TI Liquid chromatography-mass spectrometry assay of a thiadiazole derivative in mice: Application to pharmacokinetic studies.
AU Wong, Hong; Jia, Lee [Reprint author]; Camden, Jim B.; Weitman, Steve D.
CS Institute for Drug Development/CTRC, 14960 Omicron Drive, San Antonio, TX, 78245, USA ljia@saci.org
SO Journal of Chromatography B, (5 December, 2001) Vol. 765, No. 1, 55-62.
AB Modern atmospheric pressure ionization (API) ion-trap mass spectrometry in connection with fast chromatographic separations using a short narrow-bore C8 column was developed to determine 5-phenyl-3-thioureido-1,2,4-thiadiazole (301029), a novel virus inhibitor in serum. Both 301029 and an internal standard (I.S.) were separated from serum samples by acetonitrile deproteinization and extraction without time-consuming reconstitution. The chromatographic separation was achieved on a C8 reversed-phase narrow-bore column using acetonitrile-water-acetic acid (90:10:0.01, v/v/v) as a mobile phase. The mass spectrometric analysis was performed by atmospheric pressure chemical ionization (APCI) mode with positive ion detection. Single ion monitoring (SIM) scan mode of m/z 237 and 158 was used to quantitatively determine 301029 and I.S., respectively. The low limit of quantitation was 25 ng/ml. The assay exhibited a linear range of 25-2500 ng/ml. Recovery from serum proved to be 100-113%. The precision (C.V.) and accuracy (RE) of the method were 2-12% and 94-112%, respectively. The present method was applied to determine the pharmacokinetic parameters of 301029 following oral administration of the agent to mice at 5 g/kg. The results revealed

that the elimination half-life of 301029 was 413 min and the area under serum concentration-time curve was 354 mug/ml/min.

L15 ANSWER 43 OF 90 CA COPYRIGHT 2008 ACS on STN
AN 132:216478 CA
TI Higher Throughput Bioanalysis by Automation of a Protein Precipitation Assay Using a 96-Well Format with Detection by LC-MS/MS
AU Watt, Alan P.; Morrison, Denise; Locker, Karen L.; Evans, David C.
CS Neuroscience Research Centre, Department of Medicinal Chemistry (Drug Metabolism Section), Merck, Sharp and Dohme Research Laboratories, Harlow, Essex, CM20 2QR, UK
SO Analytical Chemistry (2000), 72(5), 979-984
AB Generic methodol. for the automated prepn. and anal. of drug levels in plasma samples within a drug discovery environment was achieved through the redesign of a protein pptn. assay to a microtiter (96-well) plate format and the application of robotic liq. handling for performance of all transfer and pipetting steps. Validation studies revealed that the application of robotics to sample prepn., in general, maintained the anal. accuracy and precision compared with prepg. samples manually. The use of rapid gradient LC-MS/MS for anal. coupled with flow diversion of the solvent front allowed the introduction of protein-pptd. samples into the mass spectrometer without the necessity for source cleaning. The problem inherent in automatically pipetting plasma, caused by fibrinogen clots, was overcome by storing samples at -80 °C and thus precluding clot formation. The resulting methodol. allowed sample prepn. for a 96-well plate designed to accommodate 54 unknowns, duplicate 12-point calibration curves, and 6 sets of quality controls at three levels in approx. 2 h. This approach allowed an increase in throughput of sample prepn. and anal. to >400 samples per day per LC-MS/MS instrument with minimal manual intervention. Overall, substantial time savings were realized, demonstrating that automation is an increasingly essential tool in a drug discovery bioanal. environment.

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STN INTERNATIONAL LOGOFF AT 10:55:39 ON 03 JUN 2008